properties. This is followed by a period in which the stability of the bulk active ingredient and its associated formulations is *assessed* and an expiry period established. Subsequently, stability studies are initiated and continued to *confirm and expand* the results of the preceding studies. Finally, the stability of the marketed product is *periodically reassessed*.

Thus, the development of an understanding of the stability performance of a given formulation is basically an evolutionary process. For convenience of discussion, this evolutionary progression may be divided into six stages (1):

Preformulation stage
Formulation development stage
Proposed product stage
New product stage
Established product stage
Revised product stage

Within this progression from profile to assessment, through confirmation and expansion, and finally to periodic reassessment of product stability, a range of testing protocols, methods, and mathematical models may be utilized, with each successive stage designed to augment the data base of the product and, thereby, strengthen and expand the conclusions reached during each preceding stage. At each stage differing types and amounts of information are sought that are important to the assignment of an expiry period, thus, giving rise to widely differing concerns and objectives for each phase of the overall stability-testing program.

It is also important to understand the relationship between these stages and the progression of the product through clinical development to marketing (Table 1). The evolution of the product stability performance profile begins with the preformulation stage, which is associated with the pre-IND phase, then proceeds to formulation development which is generally associated with Phase I and II clinical trials. From there it proceeds to the proposed product stage, which is temporally associated with Phase III clinical trials. The new product stage is associated with scaleup, process validation, and approval and is followed by the established and revised product stages, which are associated with the marketing of the product. Note that the timing relationships given in Table 1 represent a general approach and are not intended to be rigidly interpreted.

As the product progresses through the various stages, different kinds of studies are carried out to meet a variety of objectives. There are a number of elements that are common to all of these stability studies and that must be included in the study protocol.